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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,087	FULLER, JAMES	
	Examiner	Art Unit	
	MICHELLE S. HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *85-132* is/are pending in the application.

5a) Of the above claim(s) *94,95,104-108,114,115,117-123,129,130 and 132* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *85-93, 96-103, 109-113, 116, 124-128, 132* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication filed 7/18/2011.

Any rejection(s) and/or objection(s) not reiterated herein have been withdrawn.

Election/Restrictions

Newly submitted claim 132 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 132 is directed to a non-elected species, a 3'UTR of a simian CMV IE gene sequence.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 132 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 109-113 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Catchpole (WO 02/36792-cited by IDS) and Nott et al. (*RNA*, 2003-see attached 892 form).

The claims are drawn to (in part): a nucleic acid construct comprising a chimeric promoter sequence and a cloning site for insertion of a coding sequence in operable linkage with the chimeric promoter, wherein the chimeric promoter sequence comprises:

(a) an hCMV immediate early promoter sequence;

(b) exon 1 and at least a part of exon 2 of the hCMV major immediate sequence early gene; and,

(c) a heterologous intron provided instead of the intron A region of the hCMV major immediate early gene, wherein the heterologous intron is not positioned between the exon 1 and the at least a part of exon 2 in (b).

Catchpole describes DNA vectors derived from hCMV immediate early gene which includes exon 1 and a heterologous intron that replaces the natural intron A of HCMV IE1 (see p. 2, lines 1-8). The author further describes including a part of HCMV IE1 exon 2 (p. 4, lines 3-10). Note that this meets "a chimeric promoter" as defined by parts (a)-(c) in claim 109. Catchpole describes including restriction sites in the vector for the insertion of a heterologous coding sequence and operably linking a sequence encoding a recombinant polypeptide to the promoter (see p. 4, lines 35+ to p. 6, lines 1-10); this meets the limitation of "cloning site" as required by claim 109. The author provides coating the vector onto a gold bead (elected species H), delivering the vector via a gene gun, a syringe or a needle-free delivery approach and using a pharmaceutically acceptable carrier (see p. 16 and claim 11 of this reference and instant claims 110-113). It is noted here that the author provides the following recitation: "The vector may further include restriction sites to allow for insertion of a heterologous coding sequence. The restriction sites will preferably be positioned downstream of the HCMV IE1 5' untranslated fragment, including any heterologous intron which may be included in the vector"; see p. 4 (bottom) and p. 5 (top of the page).

Catchpole does not *explicitly* teach wherein the heterologous intron is not positioned between the exon 1 and the at least a part of exon 2 in (b); see part c of instant claim 109. Separately, Catchpole does not explicitly teach an isolated or purified DNA; see claim 116.

Nott et al. provides an analysis of intron effects on mammalian gene expression; see whole document. The authors teach that varying the position of a single intron leads to differential expression of a gene in a mammalian cell (p. 610, col. 2, Figure 2B and C and p. 613, col. 1).

Thudium discloses a method for isolating/purifying DNA constructs; p. 23, para. 3.

It would have been obvious to one of ordinary skill in the art at the time of the invention to vary the position of an intron in the method taught by Catchpole. One would have been motivated to do so for the advantage of modulating/optimizing gene expression as shown by Nott et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to purify the nucleic acid constructs taught by Catchpole. One would have been motivated to do so for the gain of optimizing results and minimizing contamination.

There would have been a reasonable expectation of success given the underlying materials and methods are widely known and commonly used as evidenced by the applied prior art (e.g. basic molecular biology techniques, construct preparation, etc.). The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claims 85-93 and 96-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of WO 02/36792 (hereinafter as "Catchpole", published 5/10/2002-cited by IDS), Nott et al. (*RNA*, 2003-see attached 892 form), WO 02/031137 (hereinafter as "Thudium"-cited by IDS), Li et al. (Gene Therapy, 2001-previously cited), US Patent 6165477 (hereinafter as "Ivy"), and Palmiter et al. (*PNAS*, 1991-previously cited) as further evidenced by GenBank Accession AF143308 (1999-see attached 892), PGPUB 20030124523 (hereinafter as "Asselbergs"-previously cited) and PGPUB 20030175711 (hereinafter as "Renner" -previously cited).

Claim 85 and its dependent claims are drawn to (in part): A nucleic acid construct comprising:

(i) a chimeric promoter sequence which comprises:

(a) an hCMV immediate early promoter sequence;

(b) exon 1 and at least a part of exon 2 of the hCMV major immediate early gene; and

(c) a heterologous intron provided in place of the intron A region of the hCMV major immediate early gene, wherein the heterologous intron is not positioned between the exon 1 and the atleast a part of exon 2 in (b);

(ii) a coding sequence in operable linkage with the chimeric promoter;

(iii) a non-translated leader sequence which is selected from the HBVpreS2 antigen sequence, HBV e-antigen sequence and HSV type 2gD antigen sequence and which is in operable linkage with the chimeric promoter; and

(iv) an enhancer sequence which is derived from a 3' untranslated region (UTR) of a HBsAg sequence or of a simian CMV immediate early gene sequence, which is in operable linkage with the chimeric promoter and which is downstream of the coding sequence.

Catchpole describes DNA vectors derived from hCMV immediate early gene which includes exon 1 and a heterologous intron that replaces the natural intron A of HCMV IE1 (see p. 2, lines 1-8). The author further describes including a part of HCMV IE1 exon 2 (p. 4, lines 3-10). Note that this meets "a chimeric promoter" as defined by at least parts (a)-(c) in claim 85 and the sequence comprising structural limitations of claim 116. Catchpole describes including restriction sites into the vector for the insertion of a heterologous coding sequence and operably linking a sequence encoding a recombinant polypeptide to the promoter (see p. 4, lines 35+ to p. 6, lines 1-10 and part (ii) of claims 85 and claim 90). The author provides coating the vector onto a gold bead (elected species H), delivering the vector via a gene gun, a syringe or a needle-free delivery approach and using a pharmaceutically acceptable excipient (see p. 16 and claim 11 of this reference and instant claims 96-102).

Catchpole does not describe using a hterologous intron that is not positioned beteewn the exon 1 and the at least a part of exon 2 (see claim 85, part (i)(c)), a non-translated leader sequence which is HBVpreS2 antigen sequence (see claim 85, part (iii)), an enhancer sequence derived from 3'UTR HBsAg sequence (see claim 85, part (iv)), a rabbit beta-globin gene (claim 87, part (ii)), an HBVsAg antigen (elected species G), the enhancer sequence which is the sequence set forth by SEQ ID NO: 8 (HBV

enhancer; elected species B and claim 86, part (iv)), a heterologous intron comprising the rat insulin intron A (elected species C) or a human tissue plasminogen activator secretion signal peptide (elected species F).

Nott et al. provides an analysis of intron effects on mammalian gene expression; see whole document. The authors teach that varying the position of a single intron leads to differential expression of a gene in a mammalian cell (p. 610, col. 2, Figure 2B and C and p. 613, col. 1).

Thudium discloses the use of a construct for the expression of a heterologous coding sequence in the pCMVkm-Luciferase in which the rabbit beta-globin gene was incorporated (see Example 2, p. 35); this meets the limitation of further incorporating one or more sequences which is a rabbit beta-globin gene (claim 87, part (ii)). The authors disclose that when the optimized rabbit beta-globin gene was used, this construct showed 4 times higher in the expression of p55 gag as compared to the parent vector; given the successful expression of p55 gag, this gene must be in operable linkage with the chimeric promoter. Note that p55 gag meets the limitation of a viral antigen (see claims 90-92) and a construct. The author also provides that the polypeptide sequences encoding proteins may include HBV antigens including the sAg/preS2 combination (see p. 21, para. 1; instant claims 85 (iii) and (iv) and 91-93; and elected species G). The author further describes techniques for isolating DNA (p. 23, para. 3 as required by claim 116). Asselbergs is cited for teaching the sequence set forth by SEQ ID NO: 10 which inherently encodes the rabbit beta-globin gene (see SEQ ID NO: 1 of this application; elected species E). Renner is cited for teaching the

sequence set forth by SEQ ID NO: 5 which inherently encodes HBVpreS2 (see SEQ ID NO: 133 of this application; elected species A).

Li et al. describe a nucleic acid construct comprising a promoter sequence, a coding sequence and a simian virus 40 (SV40) enhancer wherein the coding sequence is heterologous to the SV40; see abstract and Figures 2 and 3, p. 496. It is further noted that the authors describe administering such construct to a subject; see p. 495, col. 1, para. 3. The authors disclose that incorporation of this enhancer enhances gene expression (see title). GenBank Acession No. AF143308 (1999) is cited for providing this enhancer and its known sequence set forth by SEQ ID NO: 8, elected species B.

Ivy teaches using the human tissue plasminogen activator secretion signal sequence for secretion of protein products from Drosophila cells so that the secreted products can be easily purified and prepared as a vaccine (col. 6, lines 40+).

Palmiter et al. teaches that heterologous introns can enhance expression of transgenes in mice (see title). The authors provide that insertion of heterologous intron A of the rat insulin II gene increased expression by 75-fold (p. 480, col. 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to vary the position of an intron in the method taught by Catchpole. One would have been motivated to do so for the advantage of modulating/optimizing gene expression as shown by Nott et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to further incorporate various elements in the construct taught by Catchpole, including an SV40 enhancer sequence, intron A of the rat insulin gene and a rabbit

beta-globin gene. One would have been motivated to do so because the prior art teaches that such incorporation leads to successful or enhanced expression of polypeptides. There would have been a reasonable expectation of success, given the prior art demonstrates such success and the underlying techniques are widely known and commonly used as shown by the prior art.

It would have been obvious to one of ordinary skill in the art at the time of the invention to further incorporate various elements in the construct taught by Catchpole, including the known sAg/preS2 combination taught by Thudium. One would have been motivated to do so in order to express this known combination as a substitute antigen. There would have been a reasonable expectation of success, given the underlying techniques are widely known and commonly used as shown by the prior art.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a sequence encoding the human tissue plasminogen activator secretion signal sequence in the construct taught by Catchpole. One would have been motivated to do so for the advantage of purifying and preparing the expressed protein as a vaccine in Drosphila. There would have been a reasonable expectation of success because this signal peptide is well known and commonly used as demonstrated by the prior art.

The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Claim 103 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of WO 02/36792 (hereinafter as "Catchpole", published 5/10/2002-

cited by IDS), Nott et al. (*RNA*, 2003-see attached 892 form), WO 02/031137 (hereinafter as "Thudium"-cited by IDS), Li et al. (Gene Therapy, 2001-previously cited), US Patent 6165477 (hereinafter as "Ivy"), and Palmiter et al. (*PNAS*, 1991-previously cited) as further evidenced by GenBank Accession AF143308 (1999-see attached 892), PGPUB 20030124523 (hereinafter as "Asselbergs" -previously cited) and PGPUB 20030175711 (hereinafter as "Renner" -previously cited) as applied to claims 85-93 and 96-102 above, and further in view of Scharton-Kersten et al. (*Infection and Immunty*, 2000-previously cited).

The claim is further drawn to a composition of claim 102 which further comprises an additional construct comprising a coding sequence which encodes a polypeptide which an ADP ribosylating bacterial subunit A and B (elected species I).

The combination of Catchpole, Nott, Thudium, Li et al., Ivy and Palmitter et al. (as further evidenced by GenBank Ac. No. AF143308, Asselbergs and Renner) teach (in part): a nucleic acid construct comprising:

(i) a chimeric promoter sequence which comprises:

(a) an hCMV immediate early promoter sequence;

(b) exon 1 and at least a part of exon 2 of the hCMV major immediate early gene; and

(c) a heterologous intron provided in place of the intron A region of the hCMV major immediate early gene;

(ii) a coding sequence in operable linkage with the chimeric promoter;

(iii) a non-translated leader sequence which is selected from the HBVpreS2 antigen sequence, HBV e-antigen sequence and HSV type 2gD antigen sequence and which is in operable linkage with the chimeric promoter; and

(iv) an enhancer sequence which is derived from a 3' untranslated region (UTR) of a HBsAg sequence or of a simian CMV immediate early gene sequence, which is in operable linkage with the chimeric promoter and which is downstream of the coding sequence.

The combination of Catchpole, Nott, Thudium, Li et al., Ivy and Palmiter (as further evidenced by Moriarty et al., Dean et al., Asselbergs and Renner) does not teach the composition of claim 102 which further comprises an additional construct comprising a coding sequence which encodes a polypeptide which an ADP ribosylating bacterial subunits A and B (elected species I).

Scharton-Kersten et al. disclose that a bacterial LT composed of A and B subunits and the ADP-ribosylation activity have known adjuvant function (p. 5308, col. 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate other constructs comprising sequences encoding polypeptides known to have adjuvant activity, such as ADP ribosylating bacterial subunits A and B, in the composition disclosed by Catchpole, Nott, Thudium, Li et al., Ivy and Palmiter (as further evidenced by GenBank Ac. No. AF143308, Asselbergs and Renner). One would have been motivated to do for the gain of optimizing results (i.e. increase an immune response). There would have been a reasonable expectation of success given the

underlying techniques are widely known and commonly used as shown by the prior art references applied. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Response to Arguments

Applicant's arguments filed 7/18/2011 have been fully considered but they are not persuasive. It is noted that the arguments related to the rejections above are based upon the combined teachings of Catchpole and Nott. Thus, given they are similar in content; the arguments are addressed together below.

Applicant argues that the teachings by Nott only provide inserting an intron inside the ORF and that the recited intron of the claim is part of the chimeric promoter, i.e. outside the ORF, thereby enabling the construct in the present invention to express intact proteins, not "fusion proteins" from ORFs comprising the recited intron itself.

In response, the claims do not require that all segments of the promoter be contiguous segments nor do the claims require that all promoter segments not contained within the ORF. The claim *merely* requires that "the heterologous intron is not positioned between the exon 1 and the at least a part of exon 2". Nowhere in the claim is a specific location required for the intron other than not positioned between exon 1 and 2. Also note para. [0123] of the instant specification defines a "promoter" but does not exclude a promoter from having non-contiguous segments or a promoter segment from being positioned with an ORF.

It is noted that Nott does not teach making fusion proteins comprising intron amino acid sequences. Instead, the teachings describe luciferase activity and mRNA

level enhancement yielded by intron-containing constructs. It is not clear where in the reference the author teaches fusion proteins comprising introns, not exons. Nott was cited for teaching using a heterologous intron and enhancement of mRNA levels.

Applicant alleges that Catchpole teaches away from a combination with Nott because Catchpole teaches that a promoter comprising a heterologous intron between exons 1 and 2 has "enhanced expression." Applicant thus concludes that Catchpole would *discourage* a person skilled in the art from applying the teachings of Nott in varying the position of the intron in Catchpole's construct.

This is not found persuasive. Applicant has not demonstrated a teaching away-a teaching that a particular combination will not work. For example, Catchpole does not describe insertions of intron in other positions than between exons 1 and 2 or such insertions will not work. Thus, the argument is not clear.

Given the arguments are not found to be persuasive, the rejections above are maintained.

Claim Rejections - 35 USC § 102-Necessitated by Amendments

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 124 and 131 are rejected under 35 U.S.C. 102(b) as being anticipated by Vannice *et al.* (*J. Virology*, 1988-cited by form 892) as evidenced by Bulla and Siddiqui (*J. Virology*, 1988-previously cited).

Claim 124 is directed to: a nucleic acid construct comprising:

(i) a promoter sequence;

(ii) a coding sequence operably linked to the promoter sequence (i); and

(iii) an enhancer sequence located downstream of the coding sequence (ii) and operably linked to the coding sequence (ii);

wherein the enhancer sequence (iii) is derived from a 3'UTR of an HBsAg sequence and the coding sequence (ii) is heterologous to the enhancer sequence (iii).

Vannine *et al.* describes a nucleic acid construct comprising: (i) a promoter sequence (SV40 early promoter); a coding sequence operably linked to the promoter sequence (murine *dhfr* gene); and, an enhancer sequence comprising a 3' sequence of the HBsAg sequence; see p. 1307, col. 1, para. 5 and p. 1309 for Figure 3 and the corresponding legend disclosing the downstream positioning of the enhancer relative to the coding sequence. It is noted that given that the *dhfr* coding sequence is a murine gene, the claim limitation that the coding sequence is heterologous to the enhancer sequence derived from hepatitis B virus is met.

Bulla and Siddiqui is only cited for teaching that the HBsAg enhancer sequence is inherently located in the 3' untranslated region (3'UTR) of the HBsAg gene; see p. 1437, col. 2, para. 2.

Lastly, it is noted that the coding sequence must be operably linked to the promoter sequence and the enhancer must be operably linked to the coding sequence, given Vannice et al. teaches that the *dhfr* is successfully expressed and that the 3'UTR HBsAg enhancer sequence successfully enhances the expression of the gene; see abstract. Also see para. [0124] of the instant specification which defines the term "operably linked" as referring to an arrangement of elements wherein the components are configured as to perform their usual function.

Thus, Vannice *et al.* anticipates the claimed invention.

Claim Rejections - 35 USC § 103-Necessitated by Amendments

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 124-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Vannice *et al.* (*J. Virology*, 1988-cited by form 892) as evidenced by Bulla and Siddiqui (*J. Virology*, 1988-previously cited) in further view of Catchpole (WO 02/36792-cited by IDS).

As discussed above, Vannice *et al.* (as evidenced by Bulla and Siddiqui) teach the limitations of claims 124 and 132 which are directed to: a nucleic acid construct comprising:

(i) a promoter sequence;

(ii) a coding sequence operably linked to the promoter sequence (i); and

(iii) an enhancer sequence located downstream of the coding sequence (ii) and operably linked to the coding sequence (ii);

wherein the enhancer sequence (iii) is derived from a 3'UTR of an HBsAg sequence and the coding sequence (ii) is heterologous to the enhancer sequence (iii).

Vannice *et al.* do not teach coated particles which comprise carrier particles coated with a nucleic acid construct (claim 125); a dosage receptacle for a particle mediated deliver device comprising coated particles (claim 126); a particle mediated delivery device laded with coated particles (claim 127); and, a pharmaceutical preparation comprising a nucleic acid construct and a pharmaceutically acceptable excipient (claim 128).

Catchpole teaches the administration of nucleic acids via coating a nucleic acid vector onto a gold bead (elected species H; see instant claim 125), delivering the vector via a gene gun or a syringe (see claims 126 and 127) and using a pharmaceutically acceptable excipient (see claim 128); see p. 16 and claim 11 of this prior art reference.

It would have been obvious to one of ordinary skill in the art to further incorporate using coated particles, a dosage receptacle, a delivery device or a pharmaceutical acceptable excipient in combination with the vector taught by Vannice *et al.* (as evidenced by Bulla and Siddiqui). One would have been motivated to do so because the administration methods are known and well-described as evidenced by the applied prior art. Further, one would have been motivated to do so for the gain of optimizing results with the result effective parameter of modifying an immune response. The invention as

a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 85-93, 96-103, 109-113, 116, 124-128 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 115-123, 126, 132-133 and 137-156 of copending Application No. 11/815, 278. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to nucleic acid constructs that comprise similar elements including a chimeric promoter, encoded viral antigens, HBVpreS2 sequence, a 3' UTR sequence from a simian CMV immediate early gene sequence, ADP ribosylating bacterial toxin subunits, rat insulin gene intron A sequence, carrier particles which are gold particles and uses thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed 7/18/2011 have been fully considered but they are not persuasive. Applicant requests that this rejection is held in abeyance. Until all of the rejections and objections have been properly addressed, this rejection is maintained for reasons of record.

Conclusion

No claim is allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE S. HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ZACHARIAH LUCAS can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/M. S. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Supervisory Patent Examiner, Art Unit 1648